OBJECTIVE

To discuss the emerging concepts and applications of nanotechnology and nanoscience to the diagnosis, imaging and targeted therapy, tissue engineering and Stem Cells technologies toward cure, prevention and treatment of human diseases.

MISSION OF USF NANO-BIO COLLABORATIVE

- Promote collaborative research btw the Colleges of USF Health, and the Colleges of Engineering and Colleges of Arts and Sciences
- Support the Nanomedicine and Biomedical Engineering Initiatives of USF
- Help to create multidisciplinary education and research projects
- Develop novel approaches for translational research
- Provide new insights into nanomedicine applications for nanoscientists, clinicians and engineers in the areas of inflammatory disease, cancer, heart disease, neurological problems, drug delivery, diagnostic testing and therapeutics.

ORGANIZING COMMITTEE

- **Shyam S. Mohapatra, PhD**
  Director, Nanomedicine Research Center, Chair of NanoBio Collaborative Conference, USF
- **Ashok Kumar, PhD**
  Director, Nanomedicine Research Center, Co-Chair of NanoBio Collaborative Conference, USF
- **Robert Deschenes**
  Chair, Molecular Medicine, Associate Dean of Research
- **Paul Sanberg, PhD**
  Associate VP, Office of Research, USF
- **Shankar Sundaram, PhD**
  Director, Draper Bioengineering Center, USF

SESSION I CHAIR
Shankar Sundaram, PhD and Robert Deschenes, PhD

SESSION II CHAIR
Shyam S. Mohapatra, PhD and Thomas Webster, PhD

SESSION III CHAIR
Ashutosh Chilkoti, PhD and Ashok Kumar, PhD

SESSION IV CHAIR
Paul Sanberg, PhD and Kam Leong, PhD

March 11,2010

Dear Colleagues,

It is a great pleasure to welcome you to this USF NanoBio Collaborative Conference 2010, which is being organized for the First time at the University of South Florida. I like to especially welcome to faculty who have travelled from far and wide. The burgeoning field of nanotechnology and nanoscience, which aims to create, understand, and use nanoscale structures, devices, and systems having novel properties and functions, is expected to bring a myriad of opportunities and possibilities for advancing biomedicine. Nanotechnology research is expected to lead to a better understanding of *in vivo* intracellular interactions, intracellular transport and biomolecular dynamics, which will stimulate the development of radically new technologies that might provide novel strategies for the diagnosis and therapy of
diseases.

The fundamental concept of nanoparticles is that their actions are, in effect, the result of a series of directional, and therefore predictable, molecular recognition events. Thus, nanoparticles can be engineered such that they are designed from first principles and can therefore consist of a diverse range of chemical components presently exemplified by coordination polymers (i.e. metals, organic and inorganic ligands), polymers sustained by organometallic linkages and hydrogen bonded organic compounds. A second aspect of nanoparticle chemistry that is presently under active development is exploitation of the principles of self-assembly of natural or synthetic polymers to generate nanoscale molecules, which have pivotal biomedical applications, including diagnostics and drug delivery.

It is widely believed that *that research into the methods of engineering nanoparticles and mechanisms of nanoparticle-* mediated detection of disease cells and moleculesin vitro and in vivo will be the “holy grail” of disease detection, imaging and efficient management in 21st century.

The goal of this conference is to review and explore the latest advances in the application of nanotechnology in our different areas: nanosensors, nanomedicine, tissue engineering and stem cell technology. Our aim is to discuss te latest developments and make it as much interactive as possible.

We like to thank the financial assistance by many organization, which has maede this conference possible which includes a grant from the USF Faculty Research Council , the USF Office of Research and Innovation, USF Health Office of Research, NNRC and The Draper Bioengineering Center and the transGenex nanoBiotech Inc.

I hope you enjoy the Conference.

Shyam S. Mohapatra, PhD
Director, USF Nanomedicine Research Center
Co-Chairman, Nano-Bio Collaborative 2010

Ashok Kumar, PhD
Director, USF Nanomedicine Research Center
Co-Chairman, Nano-Bio Collaborative 2010

Nano Bio Collaborative Conference Agenda 2010

Thursday March 11, 2010

8:00AM-9:00AM- **REGISTRATION**

9:00AM-10:00AM- **Opening Remarks**

Karen A. Holbrook, PhD, Vice President for Research & Innovation and Professor of Molecular Medicine, USF, Tampa, FL

Phillip J. Marty, PhD, Associate Vice President, USF Health Office of Research,

10:00AM-12:15PM- **Session I: Nanomedicine**

Chairs: Dr. Shyam Mohapatra and Dr. Robert Deschenes

10.00AM Chilkoti Ashutosh- Protein-Polymer Nanoparticles for Delivery of Therapeutics

10.40AM Subhra Mohapatra- Targeted Nanogene Therapy for Cancers

11.20AM Don Cameron- Cell mediated drug delivery to the lungs by SNAP technology

12.00PM Thomas Webster- Nanomedicine: From Toxicity to Tissue Growth

12:40PM-1:40 PM- **LUNCH**

1:40PM-3:30PM- **Session II: Nanosensors**

Chairs. Dr. Shankar Sundaram and Dr. Andrew Hoff

1.40PM Rathneshwar Lal- Nanosensors and Devices for Diagnostics and Therapeutics

2.20PM Dale Larson– Smart medical devices

3.00PM Ahmed Busnaina- Nanoparticle Based Micro-biosensor for Early Cancer Detection

3.40PM Heather Clark-Engineering the future: Nanosensors for Biological Analysis

4.20PM Kyle Cissell- Luminescence-Based Methods for MicroRNA detection

5:00PM-6:00PM- **Poster Session– Reception**

6:30PM-8:30PM- **Dinner Symposium**

Dinner Lecture

John Sladek– Future of Stem Cells Applications

Friday March 12, 2010

8:00AM-9:00AM- **Breakfast**

9.00AM Session III: Tissue Engineering
Chairs: Dr. Heather Clark and Dr. Ashok Kumar

9.00-AM Kam Leong-Response of stem cells to nanotopography and subsequent generation of tissue-engineered blood vessel

9.40AM Jeffrey Borenstein-Nanofabrication Technology for Tissue Engineering and Regenerative Medicine

10.20AM Nathan Gallant- Cell Adhesion to Engineered Biomaterials

11.00AM Donald Haynie- Polypeptide Multilayer Nanofilms

11.40AM Sudipta Seal- Redox active nanoparticles for biomedical applications

12:20PM-1:30PM– **LUNCH**

1.30PM Session IV: Stem Cell Technology .
Chairs: Dr. Paul Sanberg and Dr. Paula Bickford

1.30PM Edward Scott-Multimodal Nanoparticles for Real Time Stem Cell Tracking

2.50PM John Sladek-Stem Cell repair in the nervous system

2.10PM Cesario Borlongan-Engineering cell therapy for CNS disorders

3.30PM Shyam Mohapatra– Stem cells in Lung Diseases

SPEAKER BIOGRAPHY
&
ABSTRACTS

Ashutosh Chilkoti
Center for Biologically Inspired Materials and Materials Systems and Department of Biomedical Engineering,
Duke University, Durham, NC, 27708-0281

Ashutosh Chilkoti received his B. Tech. in Chemical Engineering from the Indian Institute of Technology, Delhi in 1985, a Ph.D. in Chemical Engineering from the University of Washington in 1991, and was a post-doctoral fellow in the Department of Bioengineering at the University of Washington from 1992 to 1995. He was appointed as an Asst. Prof. of Biomedical Engineering at Duke University in 1996, was promoted to Associate Professor in 2002 and to Professor in 2006. He currently holds the Theo Pilkington Chair in Biomedical Engineering and currently has appointments in three departments at Duke University: Biomedical Engineering, Mechanical Engineering and Materials Science, and Chemistry. Prof. Chilkoti was awarded the CAREER award from the NSF in 1998, the 3M non-tenured faculty award in 2002, and was awarded the Distinguished Research Award from the Pratt School of Engineering at Duke University in 2003 and in 2005. He was appointed Associate Director of the Center for Biologically Inspired Materials and Materials Systems at Duke University in 2002 and Director in 2007. His areas of research include Biomolecular Engineering with a focus on stimulus responsive biopolymers for protein purification and drug delivery, and Biointerface Science, with a focus on the development of advanced coatings for control of protein and cell adhesion for biosensors and biomaterials, bioinspired nanofabrication and plasmonic biosensors. He has co-authored over 175 publications, has been cited over 5600 times, has an H-index of 44, and has 25 patents awarded or in process. He is co-founder of a start-up company (Phase Biopharmaceuticals Inc.) that has raised over $35 million in venture capital funding, and he serves on the Scientific Advisory Board of another company, Asemblon. He serves on the Editorial Board of three journals: Journal of Biomedical Materials Research, Protein Engineering, Design and Selection, and Biointerphases and is a reviewer for over 20 journals .

Protein-Polymer Nanoparticles for Delivery of Therapeutics

I will, in my first example, describe a class of protein-polymers –artificial recombinant polypeptides– that spontaneously undergo self-assembly upon conjugation to the cancer chemotherapeutic Doxorubicin (Dox) and other small hydrophobic molecules. These chimeric polypeptides (CPs) consist of a hydrophilic, biodegradable polypeptide segment that is attached to a short Cys-rich segment. Covalent modification of the Cys residues with a structurally diverse set of hydrophobic small molecules, including Dox, leads to the spontaneous formation of nanoparticles for a range of CP compositions and molecular weights. The CP-Dox nanoparticles are ~40 nm in diameter, release drug at pH 5.0 (relevant to endolysosomal release), are taken up by cells, show subsequent localization of the drug to the nucleus, and are cytotoxic. Notably the CP-Dox nanoparticles have a four-fold higher maximum tolerated dose than free drug and induce near complete tumor regression in a murine model following a single dose.

In the second example, I will discuss a new protein-polymer conjugate with interesting pharmacological properties: I will describe two new and general routes to grow a PEG-like polymer, poly(oligo (ethylene glycol) methyl ether methacrylate) (poly(OEGMA)), with low polydispersity and high yield solely from the N-terminus or C-terminus of a protein by in situ atom-transfer radical polymerization (ATRP) under aqueous conditions, to yield site-specific (N- or C-terminal) and stoichiometric conjugates (1:1). Notably, both the myoglobin-poly(OEGMA) conjugate (N-terminal conjugate) and green fluorescent protein conjugate (C-terminal conjugate) showed a 40-50 fold increase in their blood exposure compared to the unmodified protein after intravenous administration to mice, thereby demonstrating that comb polymers that present short oligo(ethylene glycol) side-chains are a new class of PEG-like polymers that can significantly improve the pharmacological properties of proteins. We believe that this new approach to the synthesis of N/C-terminal protein conjugates of poly(OEGMA) may be applicable to a large subset of protein and peptide drugs, and thereby provide a general methodology for improvement of their pharmacological profiles.

Subhra Mohapatra, PhD
Assistant Professor
Dept of Molecular Medicine
USF College of Medicine and VA Hospital,
Tampa, Florida

Dr. Subhra Mohapatra has more than 15 years of experience in immunology and cell biology. After completing her Ph.D. in the Department of Immunology, University of Manitoba, Winnipeg, Canada, she did a National Cancer Institute of Canada Fellowship in the laboratory of Dr. Arnold Greenberg, the discoverer of NK cells, at the Manitoba Institute of Cell Biology. She then came to Moffitt Cancer Center as a post-doctoral fellow in the laboratory of Dr. Jack Pledger. In addition to her position in the Department of Molecular Medicine, she has adjunct appointments in the Departments of Internal Medicine and Interdisciplinary Oncology. She has published studies in highly ranked journals and filed two patents. Further, she is a member of the Signature Interdisciplinary Program in Allergy, Immunology and Infectious Disease (SIPAIID) and the Florida Center of Excellence for Bio-Molecular Identification and Targeted Therapeutics (FCoE-BITT). She also serves as the Chief Scientific Officer and a member of the Scientific Advisory Board for TransGenex Nanobiotech, Inc., and is a member of the Editorial Board for the journal "Genetic Vaccines and Therapy". Her research focuses on targeted drug delivery in cancers and the diagnostic applications of nanohole sensors. Her work is currently funded by the National Institute of Health, the Office of Naval Research and the Florida Department of Health.

Targeted Nanogene Therapy for Cancers

There has been a wave of technological advances on the nanotechnology and nanoscience fronts, which includes advances in targeted drug delivery applications. Several classes of nano materials, including gold shells, carbon nanotubes, dendrimers, lipids and polymers, are being investigated as matrices for developing multifunctional nanoparticles that not only carry the drug payload but also contain the targeting and imaging moieties. A myriad of specific cell targeting approaches are being used, which includes not only antibodies but also small molecular ligands, peptides and other biologics. We have been investigating delivery of genes and small interfering RNAs (siRNAs) using a polycationic biodegradable polymer, chitosan, and its derivatives. Examples of successful applications of combined genomics and nanotechnology for cancers, with a particular focus on delivery of polynucleotides to prostate, lung and ovarian tumors, will be discussed.

Don F. Cameron, PhD
Professor of Medicine
Department of Pathology & Cell Biology

Don F. Cameron, Ph.D. graduated from the University of the South "Sewanee" (1969, B.S., Biology) and the Medical University of South Carolina in Charleston SC (1972, M.S., Anatomy; 1976, Ph.D., Anatomy). After spending a year at Texas Tech University College of Medicine he joined the faculty of Anatomy and Cell Biology at the University of Florida (1977) and eventually the faculty of Anatomy at the University of South Florida College of Medicine (1986). He is currently Professor in the Department of Pathology & Cell Biology with joint appointments in Neurosurgery and Chemical & Biomedical Engineering. He is a member of the USFCOM Graduate Research Faculty, the USF Diabetes Center and the Florida Center of Excelence for Biomolecular Identification and Targeted Therapeutics (FCoE-**BITT)**.

Dr. Cameron's research interests are related to normal and abnormal testicular function with focus on Sertoli cells. His major funding has been from NIH to study male infertility associated with diabetes, hyper-prolactinemia and varicocele and from NASA to study Sertoli cell mediated pancreatic islet transplantation therapy for diabetes and cell transplantation therapy for neurodegenerative diseases such as Parkinson's and disease. His current focus is the therapeutic application of extra-testicular Sertoli cells to cell transplantation therapy and cell-mediated therapeutic applications such as targeted drug delivery.

For over 30 years his primary teaching effort has been in medical Gross Anatomy. Additionally, Dr. Cameron has been a member of numerous Institutional and Profession Scientific committees and associations including membership on the Executive Council of the American Society of Andrology, member and Chairman of its Student Affairs Committee, Director of its Placement Service, and a member of its Publications Committee. He is the past president of the USF College of Medicine faculty.

Cell mediated drug delivery to the lungs by SNAP methodology

Chitosan nanoparticles are effectively used to deliver drugs to the lungs by inhalation methology for asthma and COPD. Delivery of drug-containing nanoparticles to the deep lung in this way, however, is poor (~10-30%) and difficult to control especially when there are obstructive airway issues. To overcome these limitations, isolated and pre-labeled rat Sertoli cells were pre-loaded with labeled chitosan nanoparticles which contained the anti-inflammatory compound curcumin. The pre-loaded, pre-labeled SCs were injected intravenously into a mouse model of inflammatory lung disease. At 15 minutes post-injection SCs were distributed throughout the deep lung whereas at one hour post-injection, intact Sertoli cells were absent. At one hour post-injection most of the curcumin load (>90%) was present and distributed throughout the lungs. Lung specific delivery of curcumin-coupled nanoparticles was achieved based on the positive UV spectroscopic assay unique for SCs, nanoparticles and curcumin. By 24 hours post-injection, perivascular inflammation in the lungs was absent in mice treated with curcumin delivered by the Sertoli-Nanoparticle (SNAP) drug delivery protocol. Results identify a quick and efficient methodology (SNAP) for delivering drugs to the deep lung.

Don Haynie, PhD
Associate Professor
Nanomedicine and Bionanotechnology Laboratory
Department of Physics
University of South Florida
Associate Editor, Nanomedicine: Nanotechnology, Biology, and Medicine

Don Haynie joined the Department of Physics at USF in 2009, some years after having earned his BS in physics at the same institution. His doctorate is in biophysics from Johns Hopkins University, where he was an NIH pre-doctoral fellow. He was then an NSF post-doctoral fellow at University of Oxford in Oxford Centre for Molecular Sciences. He has held other full-time academic positions at University of Manchester Institute of Science and Technology and Louisiana Tech University, and courtesy positions at University of Central Michigan and University of Connecticut School of Medicine. He is an editor of *Nanomedicine: Nanotechnology, Biology, and Medicine* and a co-editor of a forthcoming issue of *Journal of Nanoscience and Nanotechnology*. He was an invited participant in the NSF-sponsored Joint Indo-US Workshop on Futuristic Manufacturing in Kanpur, India, and a co-organizer of NanoSMat 2009, a scientific conference held recently in Rome. He founded Artificial Cell Technologies and BioLaminex. Current work in his academic laboratory concerns multilayer nanofilms, electrospun nanofibers, drug delivery and drug discovery.

Polypeptide Multilayer Nanofilms

Polyelectrolyte multilayer films are nanostructured materials. Prepared by a process of extraordinary versatility and simplicity, the films are usually built up by repeated successive dipping of a solid support in solutions of polycation and of polyanion. Polymer adsorption and complexation with oppositely-charged polymers on the film surface are both driven and limited by electrostatic interactions and the release of counterions to bulk solution. Film thickness is typically on the order of nanometers per layer. We are developing multilayer films made of polypeptides for applications in medicine and biotechnology. The applications include coatings for cell and tissue engineering, media for localized drug delivery from medical implant devices, and synthetic vaccines. Multiple patents on the technology have issued and others are in a late stage of prosecution. Two companies have been formed to advance the research and development effort and to commercialize the technology: Artificial Cell Technologies, located in New Haven, CT, and BioLaminex, located in Tampa. The former has been continuously funded since 2005, the latter is supported by a Bioengineering Nanotechnology Initiative SBIR grant from NIGMS.

Ratnesh Lal
Department of Bioengineering and Mechanical
and Aerospace Engineering
University of California, San Diego, CA, USA

Prof. Lal received his MS and M Phil in Physics and Biophysics from JNU in New Delhi and Ph.D. in Neurobiology from UAB. After postdoctoral training at Caltech, he was a faculty member at the University of Chicago and the University of California at Santa Barbara before assuming his current position as a Professor and the Director of the newly established Center of Nanomedicine at the University of Chicago. He is also a Professor in the Graduate Program in Biophysical Sciences and in the Committee on Cell Physiology. Prof. Lal is an authority on biomedical applications of atomic force microscopy (AFM) and nanoscale mechanics and imaging of complex biological systems. He has presented many international keynote lectures and his work has featured in many popular magazines and news media, including Time, Smithsonian and UPI. Prof Lal was the UTS Invited Professor in Sydney for their BioNanotechnology initiative and a New Zealand Government International Science Scholar. Prof Lal is on advisory board of several entrepreneurial companies, including RC Nano LLC and Be Green Packaging LLC, Research in his lab includes nanobiophysics, biomimetics, nanobiomechanics, and the development of nanotechnologies for biomedical sciences. Research in his laboratory involves the development of nanotechnologies for nanomedicine. In addition to seminal research publications in the field of bio-interface sciences and nanomedicine, Dr Lal holds several patents based upon AFM cantilever arrays, microfluidics, optoelectronics and nanotubes for medical diagnostics and medical nanodevices, nanoscale fluid behavior and new TIRF, FRET and related optical microscopy.

Nanosensors and Devices for Diagnostics and Therapeutics

Nanomedicine is about diagnosing, treatment, or prevention of diseases using science and technology at a size of molecules and structures that make and run human cells. Recent advances in nanoscience and technology are of particular relevance to major branches of Nanomedicine: nano-diagnostics, nano therapeutics and nano-bio-devices. Their applications encompass a range of capabilities that assist in - a) understanding basic mechanisms of the disease, b) examining roles of cell and tissue interactions and environmental perturbations, both internal as well as external, c) the diagnoses of diseases using nanoscale sensors and devices, d) designing therapeutics and drugs, e) designing efficient delivery of drugs and therapeutics, and f) designing nano/micro-electrical & mechanical stimulations for maintaining various body activity. I will discuss how manipulating nanoscale structures, processes and intermolecular interactions can be used for biosensing and conceptualizing nanodevices for a wide array of diagnostics and therapeutics. The platform technology for these sensors and devices includes integrated cantilevered and optical scanning probe techniques including atomic force microscopy, nanofluidics, nanochips, NanoMEMS, nanoelectronics, and wireless technology. I will give examples of how imaging structures and dynamics of protein structures provide new paradigms of diseases as diverse as Alzheimer's disease to smoking induced lung diseases. In the realm of nano-diagnostics, the greatest boon is the ability to build sensors for a variety of chemicals, chemical interactions, physical changes such as heat, electrical resistance, etc. This when combined with the small size of these devices would allow the use of chronically implanted, safe and long-lasting sensors. Along with remote sensing and interrogation capabilities, this area has great potential in revolutionizing diagnoses of a variety of diseases. For example, we have envisioned a sensor for in-vivo edema detection and quantification and in-vitro rapid high-throughput test for allergens and an array of biomarkers for cancer and inflammatory diseases. Nanodevices using advanced materials and physicochemical energy and forces, including brain-machine interface and nanoscale cordless pacemaker that can be operated with a wireless system will be discussed .

Dale Larson, PhD
Director, Biomedical Engineering Program
Draper Laboratory
Cambridge, MA

Dale Larson received his degrees in mechanical engineering from UVa and Stanford University. After time serving with ATT Bell Laboratories, Thermedics Inc., and Level 1 Technologies, Mr. Larson was director of Arthur D. Little's Clinical Instruments and Laboratory Automaton practice within the Medical Products Development Practice and the director of the Technology and Engineering Center at Harvard Medical School. His experience also includes roles as President and Chief Operating Officer of Genomics Collaborative Inc., a genomics startup. Currently, in addition to his role as Site Miner, he is the director of the Biomedical Engineering Program at Draper.

Smart Medical Devices

Nanotechnology offers the potential for new and improved products that leverage unique performance characteristics that exist only at the nanoscale. However, before nanotechnology can deliver on this potential, new products and processes must be identified that truly benefit from these unique performance characteristics. In this talk I will describe a class of medical devices that stand to benefit from a broad range of technological advances, including nanotechnology. These medical devices, integrate sensing, analysis and actuation providing closed loop control. We call them "Smart Medical Devices" and if properly defined and targeted stand to deliver healthcare outcomes that we expect will play an important role in addressing the crisis in healthcare financing.

Ahmed Busnaina
W.L. Smith Professor and Director
The NSF Nanoscale Science and Engineering Center for High-rate Nanomanufacturing (CHN)
Northeastern University
Boston, MA 02115

Ahmed A. Busnaina, Ph.D. is the William Lincoln Smith Chair Professor and Director of National Science Foundation's Nanoscale Science and Engineering Center (NSEC) for High-rate Nanomanufacturing and the NSF Center for Nano and Microcontamination Control at Northeastern University, Boston, MA. He is internationally recognized for his work on nano and micro scale defects (particulate and chemical) mitigation and removal in semiconductor fabrication. He also involved in the fabrication of nanoscale wires, structures and interconnects. He specializes in directed assembly of nanoelements and in the fabrication of micro and nanoscale structures. He served as a consultant on micro contamination and particle adhesion issues to the semiconductor industry. He authored more than 350 papers in jour-nals, proceedings and conferences. He is on the editorial advisory board of Semiconductor International, the Journal of Particulate Science and Technology. He is a fellow of the American Society of Mechanical Engineers, and the Adhesion Society, a Fulbright Senior Scholar and listed in Who's Who in the World, in America, in science and engineering, etc.

Nanoparticle Based Micro-biosensor for Early Cancer Detection

There is a need for multifunctional nanosystems for the simultaneous monitoring of a variety of biomarkers in biological fluids to assess the progress of disease, toxicity, stress, etc. Further, the use of such devices for multidrug release in real time disease treatment is an important goal. The detection of biomarkers in combination with controlled drug release represents an exciting long term application of multifunctional nanosystems. Northeastern University's NSF Nanoscale Science and Engineering Center for High-rate Nanomanufacturing (CHN) developed a new process for selective assembly of nanoparticles into designated nanotrenches to yield structures for such multipurpose devices. The covalent attachment of antibody on the PSL nanoparticles ensures the effectiveness of the chip while using a small number of particles. A fluorescent immunoassay for detection of biomarkers was developed for the Keck BioChip. A successful sandwich complex with fluorescence detection was accomplished with prostate and other cancer specific antigen, a model cancer biomarker, at physiological levels. The chip, although very small, has a detection limit that's orders of magnitude smaller than current technology. The attachment of the tiny chip (0.1 mm x0.1 mm) (smaller than a grain of sand) to the catheter followed by the assembly of the Ab coated nanoparticles, driven by microscopic vision guided micro-manipulators, are ongoing. This new nanobio chip design for biomarker monitoring is being tested in vitro and in vivo (as part of an intravenous catheter) to determine detection limits and effectiveness.

Heather Clark
Analytical Chemist, Biomedical Engineering Group
Task Leader, Optical Nanosensors

Heather Clark had some specific requirements for her job search when she finished her postdoctoral fellowship at the University of Connecticut's Center for Biomedical Imaging Technology. "I was looking for a place where I could do more than fundamental research. I wanted to be able to take a discovery through to an application," says Clark. At Draper, she found that balance: "Draper is unique. Here I can be creative and research new ideas, but then take the results and work with engineers to actually develop a usable application." Task leader on the Optical Nanosensors project, Clark has developed fluorescent polymer beads that bind to specific ions. Because intensity of fluorescence is dependent on the numbers of ions present, the beads can provide a quantitative measurement of ion flux in single cells. A number of diseases are related to ion channel dysfunction, including cystic fibrosis, and this technology can be useful for noninvasive testing of drug treatment protocols. Her team is investigating how to bind the beads to small molecules like glucose. This could lead to a new in vivo glucose measurement tool for diabetics that would eliminate blood-based glucose testing. She imagines the system as glucose-binding fluorescent beads periodically injected under the skin, like a small tattoo. A laser device attached to a watch or bracelet could read fluorescence through the skin for accurate, continuous glucose measurement. Clark believes Draper is a perfect place to conceive of and build this type of monitor: "A lot of engineering skills, particularly in microscale devices, are necessary to construct it. You need a place like Draper to address all of the components."

Engineering the Future: Nanosensors for Biological Analysis

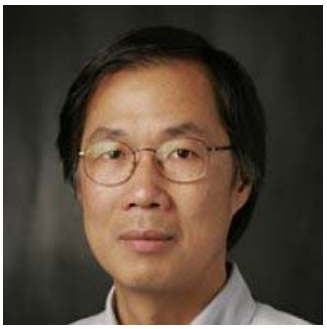
We have developed several types of nanosensors aimed at measuring ion and small molecule concentrations in the intracellular and extracellular environment. Currently, our group focuses on two applications: intracellular sodium dynamics in cardiac cells and a nanosensor "tattoo" for monitoring glucose levels in diabetics.

Diabetes mellitus refers to the group of diseases in which the body suffers from a diminished production of or resistance to insulin, which regulates the storage of glucose as glycogen in the liver and muscles. In order to avoid elevated blood sugar levels and serious health complications, diabetic patients must periodically monitor their glycemic levels throughout each day via a technique that is unfortunately both painful and inconvenient. In an attempt to address these issues, we have designed fluorescence-based nanosensors that successfully monitor glucose *in vitro* as well as *in vivo*.

Kyle Cissell
Senior Scientist
Point-of-Care Diagnostics
TransGenex Nanobiotech Inc
Tampa, FL

Kyle Cissell is currently employed at TransGenex Nanobiotech as a research scientist working on the development of point-of-care diagnostic methods for disease detection. Kyle's PhD research focused on the development of novel luminescence-based methods for microRNA detection. He has also studied the viability of intrinsically disordered proteins as biosensing systems for the detection of protein-protein interactions.

MicroRNAs (miRNA) are short, 18-24 nucleotide long noncoding RNAs. Recently, miRNAs have gained much attention due to their implication in numerous diseases. It has been found that dysregulated miRNAs are linked to disease progression. It is therefore immensely important to be able to detect these small molecules. Currently, available detection methods suffer from drawbacks including low sensitivity, being semi-quantitative in nature, time-consuming, requiring expensive instruments, etc. This work aims to develop novel miRNA technologies which will address these above problems. Four miRNA detection methods are presented which utilize luminescence-based methods. Three are based on bioluminescence, and one is based on fluorescence. The presented methods are capable of detecting miRNA from the pmole (nanomolar) level down to the fmole (picomolar) level. These methods are rapid, sensitive, simple, quantitative, can be employed in complex matrices, and do not require expensive instruments. All methods are hybridization-based and do not require amplification steps.



Kam W. Leong, PhD.
James B. Duke Professor
Director of Bioengineering Initiative
Department of Biomedical Engineering,
and Department of Surgery
Duke University
Durham, NC 27708

Kam W. Leong is the James B. Duke Professor of Biomedical Engineering at Duke University. He received his PhD in Chemical Engineering from the University of Pennsylvania and a postdoctoral training in Applied Biological Sciences at MIT. After serving as a faculty in the Department of Biomedical Engineering at The Johns Hopkins School of Medicine for 20 years, he moved to Duke University in 2006 to work on applying nanotechnology to drug, gene, immuno-, and cell therapy. He holds a Distinguished Visiting Professorship at the National University of Singapore. He serves on the editorial boards of eight journals, owns more than 40 issued patents, and has published ~230 peer-reviewed research manuscripts. The major research areas of his laboratory involve applying nanoparticles for gene delivery and understanding the response of stem cells to nanotopographical cues for stem cell tissue engineering.

Microfluidic Platforms Related to Nanomedicine

Nanotherapeutics in the form of discontinuous or continuous nanostructures can impact medicine at levels ranging from the subcellular to the tissue. Nanoparticles improve bioavailability of drugs and DNA-based therapeutics, and may achieve targeting to tissue, cell and intracellular compartments. Nanofibers and nanopatterns may dictate the response of cultured cells in tissue development. In this presentation, we will describe our attempt to apply microfluidics to synthesize polyplexes with more controllable characteristics for nonviral gene transfer. We will also discuss our recent effort to understand the influence of nanotopographical cue and fluid stress on stem cell tissue engineering as delivered by microfluidics.

Jeffrey Borenstein, PhD

Co-Program Leader, Biomaterials & Tissue Engineering, Biomedical Engineering Center, Draper Laboratory, 555 Technology Square, Cambridge, MA

Jeffrey Borenstein is a Distinguished Member of the Technical Staff at the Charles Stark Draper Laboratory in Cambridge, Massachusetts. There he serves as Technical Director for Draper's programs in Tissue Engineering and Drug delivery. He is also Program Leader for Biomaterials and Tissue Engineering with the Center for the Integration of Medicine and Innovative Technology (CIMIT), a consortium of the Harvard Medical School teaching hospitals, Draper Laboratory and MIT. Dr. Borenstein currently serves as Principal Investigator for projects involving the application of microsystems technology towards engineered tissue constructs for organ assist devices and drug discovery, as well as implantable drug delivery systems. These programs are funded by the Department of Defense, the National Institutes of Health and several commercial sponsors. Prior to joining Draper Laboratory in 1994, Dr. Borenstein held positions as a research scientist for North American Philips Corporation and Mobil Corporation. Dr. Borenstein has a Ph.D. in Physics from the University at Albany and holds sixteen issued patents, as well as over twenty-five published patent applications and over eighty peer-reviewed journal articles and conference proceedings.

Nanofabrication Technology for Tissue Engineering and Regenerative Medicine

Advances in nanofabrication technology have opened up new avenues for exploration, discovery, and the development of tools and devices for tissue engineering and regenerative medicine. Many critical processes in cells, tissues and organs involve mechanical forces and interactions occurring at the nanoscale, and nanolithographic and nanostructuring techniques have enabled replication of these interactions in the laboratory environment. The earliest applications of biological nanostructures in regenerative medicine will be tools to accelerate the development of safer and more efficacious pharmaceuticals. Ultimately, these capabilities will enable advances in organ assist devices, replacement tissues and the generation of replacement organs in the laboratory for transplant medicine.

Thomas J. Webster
Associate Professor
Division of Engineering and Department of Orthopaedics, Brown University,
Providence, RI 02912 USA
Founder, Nanovis, Inc., West Lafayette, IN 47907

Founder, Nanorose, Inc., Providence, RI 02917

Founder, NanoSeleno, Inc. Providence, RI 02917

Thomas J. Webster is an associate professor for the Division of Engineering and Department of Orthopaedics at Brown University. His degrees are in chemical engineering from the University of Pittsburgh (B.S., 1995) and in biomedical engineering from Rensselaer Polytechnic Institute (M.S., 1997; Ph.D., 2000). Prof. Webster's research explores the use of nanotechnology in numerous applications. Specifically, his research addresses the design, synthesis, and evaluation of nanophase (that is, materials with fundamental length scales less than 100 nm) materials as more effective biomedical implants. These include self-assembled organic materials which mimic the natural nanometer dimensions of tissues. Prof. Webster is the current director of the Nanomedicine Laboratories (currently at 33 members) and has completed extensive studies on the use of nanophase materials to regenerate tissues. He has graduated over 47 postdoctoral students, and thesis completing B.S., M.S., and Ph.D. students. To date, his lab group has (or will by the end of the year) generated 8 textbooks, 48 book chapters, 233 invited presentations, at least 343 peer-reviewed literature articles and/or conference proceedings, at least 504 conference presentations, and 24 provisional or full patents.

Can Tissue Engineering Benefit from Nanotechnology ?

Nanotechnology is being used to mimic structural components of tissues in synthetic materials intended for various implant applications. Recent studies have highlighted that when compared to flat or micron rough surfaces, surfaces with nanofeatures promote optimal initial protein interactions necessary to mediate cell adhesion and subsequent tissue regrowth. This has been demonstrated for a wide range of implant chemistries (from ceramics to metals to polymers) and for a wide range of tissues (including bone, vascular, cartilage, bladder, skin, and the central and peripheral nervous system). Importantly, these results have been seen at the in vitro and in vivo level. This talk will cover some of the more significant advancements in creating better vascular, cardiovascular, and orthopedic implants through nanotechnology efforts. It will also cover recent in vitro and in vivo studies which highlight better tissue regeneration. This talk will also address recent concerns of nanoparticle toxicity and the role industry has played in nanomedicine to date .

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Nathan Gallant is an Assistant Professor in the Department of Mechanical Engineering at the University of South Florida. Professor Gallant joined the USF faculty in August 2008 following a National Research Council postdoctoral fellowship at the National Institute of Standards and Technology in the Polymers Division. He graduated with a B.S. degree in Mechanical Engineering and a Cooperative Education Certificate from the Georgia Institute of Technology in 1999. He went on to earn M.S. and Ph.D. degrees in Mechanical Engineering at the Georgia Institute of Technology in 2003 and 2004, respectively, under Andres Garcia. Professor Gallant's research interests include cellular biomechanics, biomaterials, and tissue engineering.

Cell Adhesion to Engineered Biomaterials

Cell adhesion to the extracellular matrix (ECM) is central to development and the organization, maintenance, and repair of tissues by providing anchorage and triggering signals that direct cell survival, migration, cell cycle progression, and expression of differentiated phenotypes. We are investigating the biophysical, chemical and mechanical regulators of cell adhesion so that we may modulate this complex and critical process for biomaterials and tissue engineering applications. Toward characterizing the mechanical aspects of cell adhesion we have quantitatively analyzed the roles of integrin receptor binding and focal adhesion assembly in strengthening adhesion. Cell shape and adhesive contact area were engineered with micropatterning techniques to enable studies of long-term adhesion independent of cell spreading. These analyses are elucidating the contributions of focal adhesion assembly and location in strengthening adhesion. In addition, we have recently begun engineering nanofibrous ECM analogues that have controlled adhesivity for tissue engineering. These ECM analogues are fabricated by incorporating adhesion protein fibronectin into nonadhesive electrospun fibers. Thus we are able to control topographical features and cell adhesion via fibers on surfaces or in three dimensional networks.

Sudipta Seal, PhD
Professor and Director
Advanced Materials Processing Analysis Center and Nanoscience and Technology Center
University of Central Florida

Dr. S. Seal is a Professor of Mechanical Materials Aerospace Eng, and Director of Advanced Materials Processing Analysis Center and Nanoscience Technology Center (Both are academic units) since 2009 at University of Central Florida, Orlando. His research focus on regenerative nanostructures and surface engineered coatings from materials to medicine. He holds degrees in Materials Science and Eng. He is the recipient of ONR Young Investigator Award, JSPS fellow, Alexander Von Humboldt Fellow, Royal Academy of Eng Distinguished Prof @ Imperial College, London, and recently elected Fellow of American Soc of Materials, and American Association of Advancement of Science. He has published more than 250 publications, 11 patents and 3 books to his research portfolio.

Redox active nanomaterials in biomedical applications

The redox ability of ceria has been used in a wide range of applications such as three way catalysis, oxygen buffer systems and corrosion prevention. The advent of nanotechnology has opened a new field for cerium oxide in biology. Nano cerium oxide is finding potential use in the treatment of disorders caused by the reactive oxygen intermediates (ROI). This presentation will provide a brief overview of the applications of nanoceria in treatment of disorders caused by the reactive oxygen species. It is found that the scavenging property of ceria is directly linked to the retention of Ce3+ oxidation state. The role of size and stability of ceria nanoparticles in toxicity analysis has also been explored. For various practical applications, synthesis of biocompatible and stable suspensions of nanoceria is essential. It was found that the redox kinetics of ceria nanoparticles can be controlled with the type of medium and their implications in nanobiomedicine is presented.

Edward Scott, Ph.D.
Professor of Molecular Genetics at the UF Shands Cancer Center & Director of the Program in Stem Cell Biology and Regenerative Medicine,Associate Director, McKnlight Brain Institute, Univ of Florida College of Medicine, Gainsville, Florida

Edward Scott has a BA from University of Chicago and PhD in Molecular Genetics from the University of Florida. A distinguished researcher in the stem cell biology, he led a group of University of Florida researchers were able to program bone marrow stem cells to repair damaged retinas in mice, suggesting a potential treatment for one of the most common causes of vision loss in older people.

His laboratory continues to investigate the developmental linkage of these lineages and the possible existence of a common multipotent progenitor during hematopoiesis. Our basic approach to this question will be a genetic approach using murine models. We use gene targeting to generate knockout ES cell lines and animals. Students can learn (or at least see) the basics of microinjection of embryos and the production of chimeric mice. We are also adapting the PU.1-/- knockout into a model for in utero gene therapy, and determining the efficacy of PU.1 antisense oligos and ribozymes in blocking myeloid differentiation / function. (Potential therapeutic agent in arteriosclerosis). We are also investigating the role of PU.1 in the hematopoietic stem cell with a series of bone marrow transplantation experiments.

Multimodal Nanoparticles for Real Time Stem Cell Tracking

John Sladek, Ph.D
Professor of Pediatrics, Neurology, and Neuroscience
University of Colorado School of Medicine
Aurora, Colorado

John Sladek is Professor of Pediatrics, Neurology and Neuroscience at The University of Colorado School of Medicine. Previously, he served as President of California Lutheran University, Vice Chancellor for Research at the University of Colorado Health Sciences Center and Chair of Departments of Neuroscience at the University of Rochester School of Medicine and the Chicago Medical School.

Professor Sladek received his B.A. from Carthage College, where he serves as a Trustee, his M.S. from Northwestern University School of Medicine and his Ph.D. from the Chicago Medical School. He is past president of the Society for Neuroscience - Chicago Chapter and was founding President of the American Society for Neural Transplantation and Repair. He maintains an NIH-funded research laboratory studying neural repair mechanisms in a primate model of parkinsonism and a mouse model of Down syndrome. His first two scientific publications appeared in the journal *Science.* He was Editor-in-Chief of the journal *Experimental Neurology* for 15 years.

John is an accomplished jazz saxophonist and enjoys outdoor activities including cycling and nature photography.

Stem Cell Repair in the Nervous System

Over 100 million Americans and many more worldwide suffer from neurological and psychiatric disorders. The societal consequences of Alzheimer's disease alone are almost inestimable. Each year another 60,000 individuals in the U.S. are diagnosed with Parkinson's disease. There are no cures for neurodegenerative disorders and most drugs are designed to treat symptoms. Neuroprotective strategies are being developed, but may be years from being available for general therapy. Although the brain does possess some ability to generate neurons in adults this has not been shown yet to be of therapeutic benefit. Cell replacement strategies including fetal cell transplantation have shown substantial promise in animal models and some success in Parkinson's disease. Human embryonic stem cells offer considerable potential for therapy because of three extraordinary characteristics. First, they are capable of differentiating into neurons with specific identities such as transmitter type. Second, that have a unique ability to migrate to distant sites in brain and spinal cord in response to local inflammation and third, they can manufacture trophic factors to aid in neuron survival. Any or all of these qualities can be useful for repair in the nervous system. These mechanisms will be discussed with respect to specific neural problems.

Cesar V Borlongan PhD
Professor and Vice-Chairman for Research
Department of Neurosurgery and Brain Repair
University of South Florida College of Medicine

Dr. Cesar V. Borlongan is a world leader in stem cell research for stroke therapy. His highly innovative translational "bench to clinic" research has led to the world's first FDA-approved clinical trial of transplantation of cancer cell-derived NT2N neurons in stroke patients, which has reached Phase II in 2005. He has since served as the academic collaborator for a number of stem cell-based therapy companies, ensuring safety and efficacy of these novel biologics for clinical application. He previously held the position of Professor with Tenure in the Department of Neurology at the Medical College of Georgia, and served as the Director of Medical College of Georgia Neurology Cell Transplantation. He is currently a Professor and the Vice-Chairman for Research at University of South Florida Department of Neurosurgery and Brain Repair, and also holds the title of Associate Director of University of South Florida Center of Excellence for Aging and Brain Repair. He maintains an NIH Guest Researcher position.

ENGINEERING CELL THERAPY FOR CNS DISORDERS

Cesar V. Borlongan and Dwaine F. Emerich

Cell-based therapies afford varying levels of therapeutic benefits in retarding progressive neurodegeneration or stimulating regeneration after brain injury. Recent evidence provides support that biomaterials will likely enhance the functional outcome of cell therapy for brain repair. Programmable biomaterials enable and augment the targeted delivery of drugs into the brain and allow cell/tissue transplants to be effectively delivered and integrate into the brain, to serve as delivery vehicles for therapeutic proteins, and to serve as bioactive bridges for brain circuitry reconstruction. Along this vein of engineering cells to capture the brain mosaic, biomaterials acting as extracellular matrix for engraftable stem cells have additionally been explored to recapitulate specific aspects of brain niches to promote regeneration and/or repair damaged neuronal pathways. A main catalyst for this convergence of biomaterials and cell therapy is the advent of nanotechnology which allows highly regulated control over material-cell interactions that induce specific developmental processes and cellular responses including differentiation, migration, and outgrowth. Here, we discuss our own experience in the state of the art and new directions of biomaterial engineering and stem cell transplantation in the treatment of brain diseases. In particular, we present preclinical data demonstrating the efficacy and safety of transplanting encapsulated stem cells or infusion of hydrogels loaded with growth factors in relevant animal models of stroke and Huntington's disease. The long-term goal is to translate these laboratory findings to eventual clinical applications of nanoengineered stem cells for treatment of CNS disorders.

Shyam S. Mohapatra, PhD, MBA
Mabel & Ellsworth Simmons Professor
and Vice Chair of Medicine
Director, Division of Translational Medicine and
USF Nanomedicine Research Center
University of South Florida College of Medicine
Tampa, FL

Dr. Shyam (Sam) Mohapatra, a former recipient of the prestigious Alexander von Humboldt Research Fellowship and Pharmacia Allergy Research Foundation International awards, has a distinguished academic career with expertise in Molecular Biology, immunology and nanotechnology, with more than 20 years of experience in biotechnology and particularly in gene therapy and drug discovery. He has served as peer reviewer and editor for many journals and is currently the editor-in-chief of "Genetic Vaccines and Therapy". He serves as an expert in peer review panels of several major national and international grant agencies, including the NIH. He has been a consultant with and has performed collaborative and contract research for numerous pharmaceutical companies, and is on the scientific Advisry Board of Transgenex Nanobiotech Inc, which he co-founded. His research interests continues to focus on developing nanotechnology application to unraveling basic biological mechanisms underlying diseases and use nanotechnology to develop novel diagnostics and therapeutics.

NPRA Signaling in Lung Stem Cells and Tumorigenesis

Our research focuses on the role of the atrial natriuretic peptide (ANP) receptor A (NPRA) signaling in lung inflammation and cancer, specifically in the regulation of lung stem cells, when they progress from normal stem cells to cancer stem cells and eventually to malignant cancers under the influence of local inflammation. NPRA signaling promotes inflammation and tumorigenesis in mice using a variety of models. NPRA is expressed on mouse lung and bone marrow stem cells, and NPRA signaling appears to be a 'master control' pathway that regulates stem cell renewal and multipotency. These data led to the hypothesis that NPRA signaling plays a pivotal role in lung inflammation and transformation of stem cells to tumor initiating cells. By corollary, blocking of this signaling pathway might prevent neoplastic and malignant transformation of these lung stem cells (LSCs) and metastasis of lung cancers. Current research aims to characterize the effect of NPRA signaling on the self renewal and differentiation potential of LSCs and to investigate the role of host NPRA in stem cell proliferation and differentiation in inflammatory milieu .

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Graphene based miniaturized electrodes for the detection of neuro-transmitters

Subbiah Alwarappan[1], Rakesh Joshi[1], Humberto Gomez[1], Chen-Zhong Li[2] and Ashok Kumar[1]

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It is often a difficult task to detect dopamine (DA) electrochemically in the presence of other neurotransmitters such as ascorbic acid (AA) and serotonin (ST). A major reason for the foretold observation is that AA and ST are always present at a higher concentration than DA. Moreover, all of these three compounds are also oxidized at a potential similar to that of DA, which results in the overlapping of voltammetric response. Further, the electrode surface can also be readily fouled by accumulation of products from oxidation of AA and ST. Homogeneous catalytic oxidation of AA and ST by oxidized DA is another major interference in the determination of DA. Selective measurement of DA in the presence of AA and ST is therefore necessary and has become a major topic in electrochemical research. Different approaches such as Nafion ion-exchange membranes, self-assembled monolayers and organic polymers have been used to solve these problems. However, in all these methods, the immobilized layers were prone to surface deactivation due to solvent evaporation and they decay with time, resulting in non-uniform thickness and poor reproducibility. In order to overcome these issues and to selectively detect DA in the presence of AA and ST, graphene nanosheets were employed as alternate electrode materials. Results, indicated that graphene exhibited a selective and stable voltammetric detection of DA in the co-existence of AA and ST. Reasons for the observed behavior will be discussed in this presentation.

Growth and differentiation of cancer cells on three-dimensional (3D) scaffolds as a model to study tumor-stroma interactions

[1,3,4]Yvonne Davis, [1,3,4]Subhra Mohapatra, [2,3,4]Shyam Mohapatra,
[1]Departments of Molecular Medicine, [2]Internal Medicine, [3]SIPAIID and
[4]Nanomedicine Research Center, College of Medicine, University of South Florida

Cancer cells interact with stroma as a tumor grows, and both tumor and stroma co-evolve. The microenvironment of the extracellular matrix plays a crucial role in this interaction; both tumor and stroma receive topographical and mechanical cues from pores, ridges and fibers of the ECM . Most research done so far is on 2D surfaces and little is known of tumor-stroma interactions on 3D matrices . This study aimed at developing artificial 3D scaffolds with mechanical/topographical features of *in vivo* stromal matrix to study tumor-stroma interactions. Scaffolds were made by electrospinning poly(lactic-co-glycolic) acid (PLGA) nanofibers. This fibrous scaffold provides a large surface to volume ratio and high porosity for cell growth and differentiation. A different type of 3D matrix tested was made by the self assembly of oppositely charged polyelectrolytes, chitosan and alginate to form a chitosan/ alginate hydrogel . PC3 prostate cancer cells and WMPY stromal cells were cocultured on the scaffolds and proliferation was measured by WST (mitochondrial activity) and Ki67 (nuclear antigen) assays. On the PLGA scaffold, conditioned media from PC3 cultures stimulated WMPY proliferation while conditioned media from WMPY cultures stimulated PC3 proliferation. PC3/ WMPY co cultured cells showed greater proliferation than cells grown separately in conditioned media Cells cocultured on chitosan/alginate hydrogels grew slower than on the PLGA fibers indicating that differences in the architecture of the microenvironment plays an important role in tumor stroma interactions. Tumor cells growing with stromal cells on tissue-engineered 3D scaffolds provide a pseudo-*in vivo* model for studying cancer progression mechanisms and testing new anticancer agents.

Mechanical Role of Focal Adhesions in Cell–Substrate Adhesion

Kranthi Kumar Elineni, Nathan D. Gallant

Department of Mechanical Engineering, University of South Florida.

The interaction of cells with the extracellular matrix (ECM) plays a dominant role in the formation and maintenance of tissues and is primarily mediated by integrin adhesion receptors. Upon binding, these receptors recruit intracellular proteins and assemble to form structures known as focal adhesions. Focal adhesions reinforce adhesion strength and mediate signaling pathways that determine cell fate.

The overall objective of this work is to explain the mechanical role of focal adhesions in cell-substrate adhesion. Based on our observations that focal adhesions tend to form at the periphery of spread cells, we hypothesized that there is significant role of adhesive bond position in regulating overall adhesion strength. We made use of soft lithographic techniques and well defined surface chemistries to analyze the effect of bond position on the overall adhesion strength independently of the adhesive area. Cells are cultured on these micro- patterned substrates coated with adhesive proteins to control cell shape and adhesive domain. A hydrodynamic shear assay will be used to quantify the adhesion strength between the cell and the substrate. This research is expected to answer many intricate questions on cell spreading, integrin clustering, cytoskeleton interactions, and non-uniform distribution of focal adhesion complexes, which form the key factors in understanding the underlying mechano-sensory processes governing how cells interact with ECM to form a specific type of tissue.

Examining the dependency of the flexibility of type 1 molecular collagen on solvent conditions

Heather Harper, W.G. Matthews

Collagen is the most abundant protein in the body by mass. Specifically, type 1 collagen is responsible for the mechanical properties of various tissues such as tendons, ligaments, and cornea. To fully understand the mechanical properties of these large-scale structures, the study of type 1 collagen on the molecular scale is vital.

Type 1 collagen molecules are typically on the order of 300nm in length and with reported persistence lengths ranging from 14.5nm to 170nm. Clearly there exists a large discrepancy in the literature on the flexibility of these molecules. Here we present a study of the dependency of the flexibility of type 1 collagen molecules on buffering solution.

Type 1 collagen molecules are suspended in buffer solutions containing varying concentrations of NaCl. Tapping mode AFM images are taken of the molecules after deposition onto freshly cleaved mica. The contour length and end-to-end distance of the molecules are measured and the persistence length is calculated for each buffer solution using the worm-like chain model.

By examining the effects of various concentrations of NaCl, we demonstrate that the flexibility of the type 1 collagen molecule is strongly dependent upon ion concentration in the solvent. We have shown that the persistence length of the molecule ranges from approximately 10nm in DI water to approximately 80nm in a 0.1M NaCl solution. Directly quantifying this relationship will greatly aid future studies into engineering large-scale collagen tissues.

Parainfluenza virus type 3 N-terminally truncated C protein, CNΔ25, is a potent inhibitor of viral replication in mice

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Background & Objectives: Human parainfluenza viruses (HPIVs) cause serious lower respiratory tract disease with repeat infection especially among the elderly and immunocompromised patients. Currently there is no vaccine. The C protein of HPIV-3 is a multifunctional accessory protein that inhibits viral transcription and interferon (IFN) signaling. The main goal of this study was to determine the effect of a truncated C protein, CNΔ25, on HPIV-3 infection in a mouse model.

Methods: We treated mice with a CNΔ25 expression plasmid and examined the effect on HPIV-3 titers, lung inflammation and cytokine profile. BALB/c mice were treated intranasally (i.n.) with chitosan nanoparticles alone or containing pCNΔ25 or vector pcDNA3 on days 1 and 2. On day 3, the three groups of mice were given PBS (vehicle, negative control) or 7x10^6 MOI HPIV3 i.n. Mice were euthanatized on day 8 and bronchoalveolar lavage (BAL) fluid and lungs were taken. Differential cell counts in BAL fluid, histopathology in lung sections, cytokine levels and virus titers were determined.

Results: pCNΔ25-treated mice showed fewer eosinophils in BALF, less damage to lung mucosal epithelium and fewer infiltrating inflammatory cells. The HPIV-3 titer was significantly lower in pCNΔ25- treated mice compared to the vector control group. Interleukin-4, -5, and -13, IFN-g, and TNF-a were significantly decreased in pCNΔ25-treated mice.

Conclusions: Truncated C protein of HPIV-3, CNΔ25, significantly decreased virus titer and lung inflammation in a mouse model of HPIV infection. These findings suggest that CNΔ25 could be used as an antiviral agent to prevent HPIV3 infection in humans.

Keywords: Parainfluenza virus, Mouse lung inflammation.

Prototype of an energy harvesting nanogenerator implant based on ZnO nanowires

Mikhail Ladanov, Garret Matthews, Ashok Kumar

Our research is aimed at an implant prototype device with a piezoelectric element intended for gathering mechanical energy.

Based on piezoelectric ZnO nanowires embedded in a collagen matrix, the device consists of a bottom electrode with a forest of vertically aligned periodic ZnO nanowires, a matrix of collagen fibers entwined between the nanowires for mechanical stability and incorporation into tendon, and a fixed top electrode that will be rigidly attached to bone.

Investigation was done on growth characteristics of piezoelectric ZnO nanowires through chemical, VLS techniques and\or PLD. Controlled growth is required to achieve vertically aligned uniform crystalline nanowires with optimal density within the collagen matrix and to produce a defined geometric structure for incorporation in the device. Characterization includes SEM, TEM and XRD measurements to confirm crystalline structure, shape and uniformity of nanowires.

The bending rigidity and the piezoelectric response of the nanowires are being investigated through AFM force spectroscopy.

Type I collagen fibrils were formed *in situ* from molecular collagen solutions. Investigation of the effects of collagen concentration, polymerization time, and temperature of the formation of the nanowire/collagen matrix is being done, seeking strong coupling between the two phases and sufficient mechanical strength to withstand the forces experienced after implantation.

Various materials, including sputtered metals, precipitated metals, and conducting polymers, are to be used as a top contact to provide electrical and mechanical coupling to the nanowires.

CELL INTERACTION WITH FIBRONECTIN INCORPORATED INTO ELCTROSPUN NANOFIBERS

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Abstract

The physical as well as the biochemical properties of the extracellular matrix (ECM) play an integral part in the regulation of cell adhesion and cell fate determination. Thus, these factors are important design parameters for biomaterial surfaces and the fabrication of cell supports such as tissue engineering scaffold. In this study, electrospun protein scaffolds provide the architecture and biochemical composition of an ECM in which adhesion interaction via cell surface receptors can be manipulated. These interactions are vital in regulating cell survival, growth, differentiation and migration.

Nanofibers composed of the globular proteins bovine serum albumin (BSA) and fibronectin were produced by electrospinning from a solution consisting of 10% BSA, β-mercaptoethanol (BME), trifluoroethanol (TFE), deionized water $(dH_2O)_2$, and various concentrations of fibronectin. Fibers based on BSA were selected due to its abundance in blood and its non-adhesive nature. Therefore, the nanofibers produced via the spinning process are expected to resist protein fouling and non-specific adhesion. The incorporation of fibronectin is expected to support integrin receptor-mediated cell adhesion.

We will investigate the effect of denaturing by solvent and BME and incorporating into electrospun nanofibers on the bioactivity of fibronectin. Furthermore, we will demonstrate the ability to manipulate specific receptor-ligand interactions with nanofibrous scaffolds and nanostructured surfaces. Immunoassays will be used to characterize the fibronectin presentation and conformation. Fibronectin serves to organize cellular interaction with the extracellular matrix by binding to other ECM proteins and the fibronectin receptor (e.g. $\alpha_5\beta_1$) on cell surfaces, thus mediating cellular adhesion. Immunofluorescence will be used to image the integrin clustering and focal adhesion assembly.

In summary, we have embraced a biomedical engineering approach to assess the effect of adhesion protein incorporation into non-adhesive electrospun fibers and signaling. We will analyze the role that the ECM adhesion protein fibronectin plays when embedded with electrospun fibrous BSA mats, its advantageous properties with respect to integrin binding, focal adhesion, and cell integration with the ECM versus that of planar surfaces or electrospun fibers without the integration of fibronectin.

Keywords: Electrospinning, Integrins, focal adhesion, globular protein, bovine albumin, fibronectin

Biocompatibility Assessment of SiC Surfaces after Functionalization with Self Assembled Organic Monolayers

Alexandra Oliveros[1], Sebastian J. Schoell[2], Christopher Frewin[1,3], Marco Hoeb[2], Ian D. Sharp[2] and Stephen E. Saddow[1,3,4]

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Keywords: Biocompatibility, Silicon Carbide, Self Assembled Monolayers.

The integration of biological and surface modification techniques has allowed development of new platforms for improving both biomedical devices and pharmaceutical delivery technologies. Wide-bandgap semiconductors have played an important role in this field because they possess superior sensing capabilities and good biocompatibility. The use of such materials for long-term implantable devices requires a high degree of biocompatibility that implies cell surface attachment and spreading as well as a specific surface growth morphology. SiC is known to be a chemically inert and biologically-permissive substrate, making it a suitable material for the fabrication of biosensors. In this study we show that functionalization of SiC surfaces using methyl- and amino-terminal organosilanes and alkyl self-assembled molecular monolayers significantly increase the substrate's biocompatibility. We used two cell lines, H4 human neuroglioma and PC12 rat pheochromocytoma, and *in vitro* techniques to demonstrate the enhanced biocompatibility of SiC substrates following molecular surface modification. MTT, 3-*(4,5-Dimethylthiazol-2-Yl)*-2,5-*Diphenyltetrazolium Bromide*, assays were performed to determine general cell viability on each substrate. Atomic force microscopy (AFM) was used to quantify the general cell morphology on substrate surfaces along with the substrate permissiveness to cellular filopodia and lamellipodia extensions. The identified cell morphology (i.e. elongated and membrane extension) demonstrate the permissiveness of the evaluated substrates and the MTT assays show an increase in cell viability of as much as two times for the PC12 cell line and three times for the H4 cell line with respect to the untreated surfaces. These results represent a dramatic improvement in cell viability using these functionalization strategies which may be utilized for development of future biosensor and medical devices.

Curcumin-Genistein Nanocomplex: a Potent Drug for Prostate Cancer

Kejal Patel[1], Xiaoqin Wang[1], Ronil Patel[1], Vikas Sharma[1], Sandhya Boyapalle[2,3] Julio Garay[2,3], Shyam Mohapatra[2, 4] and Subhra Mohapatra[1, 4]
Departments of [1]Molecular Medicine and [2]Internal Medicine, University of South Florida College of Medicine and [3]Transgenex NanoBiotech Inc., [4]JAH-VA Hospital, Tampa

Background & Objectives: Curcumin, an ingredient of Indian curry spice, has anti-inflammatory, antioxidant and anticarcinogenic activities. It inhibits proliferation of tumor cells in culture, prevents carcinogen-induced cancers in rodents and inhibits the growth of tumors in animal models. However, curcumin is only slightly water soluble and its bioavailability is poor. Genistein is a soybean isoflavone antioxidant that inhibits tyrosine kinase activity. Prostate cancer (PCa), is the second leading cause of cancer-related death among U.S. men. Identification of nontoxic agents that delay the onset and/or progression of PCa is the goal of this project. Here we test nanocomplex formulations containing curcumin and genistein for increasing water solubility and anticancer potential to treat PCa.

Methods: We prepared curcumin-genistein nanocomplexes and tested their cytotoxic effects on different PCa cell lines and normal cells by WST proliferation assay. Apoptosis induced by curcumin-genistein nanocomplexes was determined by terminal transferase dUTP nick end labeling (TUNEL) assay and poly-ADP polymerase (PARP) cleavage.

Results: Formulation of curcumin-genistein nanocomplexes increased curcumin's water solubility and resulted in significantly greater cytotoxicity on PCa cells than curcumin alone. Treatment of PCa cells with nanocomplex caused more apoptosis than free curcumin and genistein as measured by TUNEL assay and PARP cleavage.

Conclusion: Nanocomplex formulations of a curcumin-genistein mixture show enhanced water solubility of curcumin and anticancer activity against prostate cancer cells. Nanocomplex therapy may prove to be very effective in preventing or treating PCa.

Research supported by: NIH

Natriuretic Peptide Receptor A regulates Macrophage Inhibitory Factor expression in Prostate Cancer

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Objective: We have recently demonstrated that mice deficient in atrial natriuretic peptide receptor A (NPRA-KO) cannot support the growth of implanted prostate tumor cells and downregulation of NPRA expression by siNPRA or NPRA inhibitor induced apoptosis in PCa cells and reduced tumor burden in mice. However, the precise mechanism of NPRA action in PCa remains unclear. Macrophage migration inhibitory factor (MIF), a proinflammatory cytokine, is overexpressed in prostate cancer and unique for its functions in many processes associated with tumor survival. In this study, we investigated the effect and associated mechanisms of NPRA and MIF pathways in a transgenic adenocarcinoma of mouse prostate (TRAMP) model.

Methods: In vivo expression of NPRA and MIF was checked by RT-PCR, Western blot and ELISA assay in prostate tissues of TRAMP mice as well as TR-C1 cell transplanted C57/BL6 mice. The role of NPRA deficiency in modulating MIF signaling was examined in PCa cell lines derived from TRAMP mouse prostate (TRAMP-C1) and in TRAMP-C1 xenograft treated with NPRA inhibitor.

Results: NPRA expression co-related with MIF expression in TRAMP mice during PCa progression. Downregulation of NPRA expression by siNPRA significantly reduced MIF expression. Moreover, treatment of TRAMP-C1 xenografts with NPRA inhibitor also reduced MIF expression.

Conclusion: Our results suggest that NPRA is an upstream regulator of MIF signaling during PCa progression, and NPRA promotes PCa development by modulating MIF pathway.

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Cord Blood Derived T cells Stimulate Proliferation of Adult Hippocampal Neural Stem cells

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Neurogenesis continues throughout the lifespan, but significantly decreases with age. Mononuclear cells from human umbilical cord blood (HUCB) have been shown to increase the proliferation of neural stem cells (NSCs) in the subgranular zone of aging rats; a single intravenous (i.v.) injection of HUCB cells enhances incorporation of bromo-deoxyuridine (BrdU) into proliferating cells, increased neurogenesis as determined by doublecortin immunostaining and decreased inflammation as determined with immunolabeling for OX-6 positive (+) microglia even two weeks after the injection (Bachstetter et al, BMC Neuroscience, 2008). In order to identify the cellular component of the HUCB mononuclear fraction responsible for these effects, the HUCB was fractionated into T cells using a pan T antibody, CD4+ T cells, CD8+ T cells, CD14+ monocytes/ macrophage, and CD133+ stem cell populations. The whole mononuclear fraction and these specific subfractions were cultured for 4 days *in vitro* (DIV) and the media collected. Adult rat hippocampal neural stem cells stem cells were grown under proliferating conditions with the addition of HUCB conditioned media for 6 DIV. Survival of the NSCs was determined with the fluorescein diacetate (FDA)/propidium iodide (PI) live/dead assay while proliferation was measured by BrdU incorporation. All of the HUCB-derived T cell fractions significantly increased BrdU incorporation into the NSCs ($p < 0.0001$). Survival tended to increase in those NSC cultures treated with the mixed (pan) T cell and CD8+ T cell fractions while the CD14+ and CD133+ conditioned media decreased survival. Similarities and differences between the results of this study and other reports in the literature will be examined further

Microsporidia and Microsporidiosis: An Emerging Global Public Health Problem

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Objective: Detection of microsporidia in environmental and biological samples. **Background/rationale**: Microsporidia are obligate parasitic fungi that infect a wide range of invertebrate and vertebrate species. They include 150 genera and 1200 species. Targets for the present study are species of the genus *Encephalitozoon*, which are recognized as waterborne, airborne, food-borne and zoonotic emerging pathogens infecting humans, causing a variety of non specific symptoms, referred to as microsporidiosis syndromes. The populations at risk of developing serious intestinal and/or extra-intestinal illnesses include the immunocompromised HIV-infected AIDS patients, immunosuppressed organ transplant recipients and cancer patients, and the immunodeficient young children and the elderly. Disseminated microsporidiosis has been observed in post mortem pathological analysis of AIDS patients, and organ transplant recipients and cancer patients who developed severe complications. The levels of human exposure to microsporidia are not known because current methods of isolation of microsporidian spores are not effective. **Methods**: USF proprietary methods of isolation and detection that are targeted to the chitin content in the spore wall of microsporidia were used to isolate and quantify microsporidia in environmental and clinical samples, including dust, water, and blood. Identity of the *Encephalitozoon* species was confirmed by immunological and molecular biological methods while infectiveness was demonstrated by in-vitro cell culture. **Results:** It is now possible to monitor the levels of microsporidia in the air that we breathe, our waters, and in our blood supply for transfusion. **Conclusion**: The role of environmental microsporidia on the levels of microsporidemia in humans is of global concern for public health.

Design of a Novel Drug Delivery System to Treat Ovarian Cancer

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The objective of this study is to design, fabricate, and validate a novel transuterine applicator device to deliver nanoparticle encapsulated anticancer drugs directly to the ovaries for a more effective treatment of ovarian cancer. Recognizing the severity of ovarian cancer and the limitations of current treatments, there is an urgent need for a safe and effective targeted drug delivery method for treating ovarian cancer. We propose developing a targeted nanoparticle vehicle for delivering nano-encapsulated anticancer drugs directly to the ovaries via a single-use transuterine applicator. The device is inserted through the vagina into the uterus where the drug-loaded nanoparticles are released in proximity to the ovaries, thus ensuring rapid uptake and maintenance of the therapeutic drug dose. Preliminary results show that a transuterine device that fits the dimension of the human female genital tract can be designed and developed to deliver nano -encapsulated molecules. Current research focuses on in vitro synthesis and characterization of nanoparticles using SKOV3 cells and in mice using a dummy intravaginal applicator.

Sol-Gel Column Technology for Early Diagnosis of Disease

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Developing analytical tools for early diagnosis of diseases (such as cancer and Alzheimer's) is critically important in biomedical research. Early diagnosis allows medical professionals to win the valuable time to treat the disease with high success rates. From an analytical chemistry perspective, early diagnosis of a disease translates into detection of ultra-trace quantities of the disease biomarker molecules: the lower the concentration of the biomarker(s) detected, the earlier the diagnosis. In the early stages of the disease, ultra-trace concentrations of disease biomarkers may remain below detection limit of the diagnostic instrument and the disease may go undetected. In biomedical research involving early diagnosis, one important strategy is to enrich the biomarker molecules from the original sample matrix and then analyze the enriched sample to enable the detector to "see" the biomarkers by bringing their concentrations above the instrument's detection limit. In our laboratory, we have developed sol-gel capillary microextraction (CME) [1, 2] – a solvent-free sample preconcentration technique that can be used in early diagnosis of diseases. CME can be easily hyphenated with analytical separation techniques like capillary electrophoresis (CE) or high-performance liquid chromatography (HPLC). Capillary microextraction can be applied to electrically charged as well as neutral biomarkers. In the sol-gel approach, a liquid sample containing ultra-trace concentrations of the biomarker(s) is passed through a fused silica capillary coated with an appropriate sol-gel material possessing high affinity for the biomarker(s) but not for other types of molecules that might be present in the sample. In the case of zwitterionic biomarkers, electrically charged sol-gel coatings [3, 4] are used. We have demonstrated [5] the possibility to achieve a sensitivity enhancement factor of up to 1.5×10^5 for an amino acid using a positively charged sol-gel coating. In such research, the pH needs to be manipulated within a wide range. Therefore, pH stability of the used sol-gel coating is very important in achieving the desired goal. Silica-based coatings (widely used in separation science) often fail to meet this requirement. To address this issue, we have developed titania- [6, 7], and germania-based sol-gel coatings [8] that demonstrated exceptional pH stability within a wide range (pH 0.0 – 14.0).

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Research at UNRC covers a wide spectrum of human diseases from atherosclerosis, to asthma to diabetes, traumatic brain injury and cancer. By combining the wide expertise of scientists from molecular medicine, pharmacology, physiology, pathology, anatomy, cell biology, chemistry, physics and engineering, we aim to develop novel approaches to therapy that will become the cornerstones of treatment well into the 21st century. In a collegial atmosphere, and with the best current technological resources available, the dedicated members of the UNRC welcome you to share the vision of a disease-free future and to work with them in making this a reality.

Nanomedicine

One of the main goals at the Center is the development of nanomedicine research with emphasis on fabrication and testing of ultrasensitive diagnostic devices and imaging methods for the earliest possible detection of diseases with the greatest accuracy. The application of nanomaterials and nanofabrication techniques to develop such devices and for the design and translation of cell-targeted delivery of drugs and genes is being pursued in collaboration with NNRC, the Draper Bioengineering Center and Transgenex Nanobiotech, Inc. The combined knowledge of the UNRC researchers will be utilized in the selection of biomarkers, in microfluidic device fabrication, and in applying nanotechnology to the construction of biochips for remote monitoring of a patient's condition. The Center's research will also focus on the potential of cell-specific targeting and genetic modification of therapeutic cells using nanocomplexes formulated from proprietary biomaterials such as modified chitosan, PLGA and other biocomppolymers

Tissue Engineering

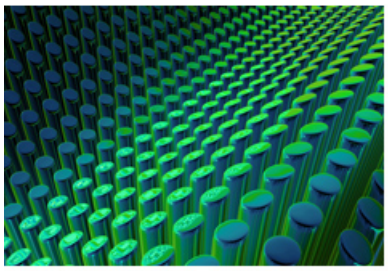
The architecture of human tissue is perfectly suited to its function. Bioengineers at UNRC attempt to harness nanotechnology to create 3-dimensional copies of skin, bone, cartilage and other tissue types with special properties. Like the natural matrix in the human body, these engineered tissues support the growth of many types of cells. The 3-D structures can be created with built-in sensors, drug release modules, chemoattractants and other modifications and implanted into the body as a means to control disease or monitor therapies. Center scientists are exploring a wide variety of new materials and nano- and micro-fabrication methods to optimize these tissue constructs for use in treating cardiovascular disease, inflammatory conditions, neurodegenerative diseases and cancer.

Cell Technology

Center scientists have been investigating the use of umbilical cord blood stem cells and Sertoli cells for cell-based therapeutic applications to diseases such as Alzheimer's, Parkinson's, ALS, brain trauma, cardiomyopathies, and cancer. Prenatal gene therapy, stimulation and mobilization of bone marrow stem cells by the atrial natriuretic peptide pathway or with granulocyte colony stimulating factor and stem cell factor are also being investigated. The former is being studied in animal models of chronic lung disease and lung cancer, while the latter is being studied in animal models of neurodegenerative diseases and in traumatic brain injury. Additional research areas will seek to understand how embryonic stem cell differentiation is regulated and how this knowledge can be translated into novel cell therapies. Other investigators are pursuing research projects with direct relevance to Alzheimer's disease and brain trauma and repair, involving monocytes or, ultimately, bone marrow stem cells as ferries for therapeutic genes. Yet another group is investigating abnormalities in the function and development of professional antigen presenting cells, or dendritic cells (DCs), the cellular and molecular mechanisms of T-cell suppression and tolerance induced because of abnormal differentiation of myeloid cells, and human testing of dendritic cell vaccines.

The University of South Florida Nanomedicine Research Center, the UNRC, was founded in 2009 at the College of Medicine to serve as a catalyst for advancing the basic and translational aspects of nanomedicine, tissue engineering and cell technologies at USF. The University is one of the fastest growing research institutions in the US according to the National Science Foundation, and the enhancement of its position through developing a nationally recognized nanotech program provides a significant boost to its research position.

Goals of the UNRC:



Research at the UNRC focuses on applying nanoparticle and nanomaterial technology and microelectronic fabrication and detection techniques to the discovery of new diagnostic and therapeutic tools. Interdisciplinary collaborations between scientists and clinicians in the College of Medicine with faculty and scientists in the Colleges of Arts and Sciences and Engineering will ensure that novel strategies and innovative approaches are used to target goals that promote the mission of USF Health while at the same time serving the broader community.

People want and need solutions now to the problems of drug-resistant pathogens, pandemic disease, increased incidence of respiratory and cardiovascular disease, Alzheimer's disease and diabetes. The members of the UNRC fervently believe that the development of new nanomaterials and fabrication methods and their application in medicine will be key to promoting worldwide health in the 21st century.

Dedication to the teaching of young scientists is also a major part of our mission. The environment at the UNRC is geared towards hands-on intensive training combined with a rigorous evidence-driven approach to research. Students are encouraged to develop a project with advice from their mentors, to utilize all the great resources of the Center, and to pursue their goals to completion and publication of results.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